REMARKS

Status of Claims

Claims 37-41, 48-57, and 73 are pending with claim 37 being the only independent claim. Claims 38, 40-41, and 52-53 are withdrawn. In order to expedite prosecution, in this Reply, claims 37-41 have been amended and claims 44-47 and 58-72 have been canceled. Support for the amendments exists, *inter alia*, in the original claims and at page 48, paragraph [0062]. No new matter has been added. Applicants expressly reserve the right to file one or more divisional applications directed to the subject matter canceled from the claims.

Applicants respectfully request the Examiner to reconsider and withdraw the rejections in view of the foregoing amendments and the following remarks.

Specification

The specification has been amended to correct the typographical error in the table at page 48, paragraph [0062]. It is clear that compound A 0.1 mg/kg i.v. + compound B ***0.3*** mg/kg i.v. was a typographical error because the text of paragraph [0062] recites that compound A in the dosage of 0.1 mg/kg intravenous ***was combined*** with compound B in the dosage of ***0.03*** mg/kg intravenous and the action of the combination was compared with that of the individual substances. Accordingly, the table now recites that compound A 0.1 mg/kg i.v. + compound B ***0.03*** mg/kg i.v. resulted in 42.5% inhibition of the rate of contractions. No new matter has been added.

Claim Rejections Under 35 U.S.C. § 103

The rejection of claims 37, 39, 48-51, 54-57 and 71-73 under 35 U.S.C. § 103(a) over Chutka et al., "Urinary Incontinence in the Elderly: Drug Treatment Options," 1998, Drugs, Volume 56, Number 4, pages 587-595 ("Chutka et al.") in view of U.S. Patent No. 6,248,737 ("Buschmann et al. '737") and Andersson et al., "The pharmacological treatment of urinary incontinence," 1999, British Journal

of Urology International, 84:923-947 ("Andersson et al.") is respectfully traversed.

According to independent claim 37, as amended, the presently claimed composition of matter comprises as an admixture at least one compound selected from group (i) and oxybutynin, wherein group (i) consists of: 1-phenyl-3-dimethylamino-propane compounds corresponding to formula I, or a salt of any of the foregoing with a physiologically tolerated acid.

Importantly, the presently recited admixture of at least one compound selected from group (i) and oxybutynin exhibits a synergistic effect for the treatment of urinary incontinence. Accordingly, the combination of at least one compound selected from group (i) and oxybutynin can be employed in a low dose with fewer side effects and/or analgesic actions. Page 4, paragraphs [0010]-[0011].

In contrast, Chutka et al. relates to drug treatment options for urinary incontinence in the elderly. Chutka et al. discloses that both anticholinergic drugs and opioids can decrease the contraction of the detrusor by impairing the contractility of the detrusor and potentially lead to urinary retention. Page 593, 3rd paragraph and Table 1.

Buschmann et al. '737 discloses 1-phenyl-3-dimethylaminopropane compounds as analgesics suitable for the treatment of pain, including (+)-(2R,3R)-1-dimethylamino-3-(3-methoxyphenyl)-2-methylpentan-3-ol hydrochloride. Abstract and Example 2.

Andersson et al. relates to treating urinary incontinence and discloses that oxybutynin is an antimuscarininc agent effective in treating detrusor hyperactivity. Page 929, 2nd paragraph.

The presently claimed composition of matter is nonobvious over the combination of Chutka et al., Buschmann et al. '737, and Andersson et al. because the presently claimed composition of matter an exhibits ***unexpected synergistic effect*** in the treatment of urinary incontinence.

Test data demonstrating the unexpected synergistic effect is found in Example 1 on pages 47-49 of the specification. In Example 1, individual administration of (+)-(2R, 3R)-1-dimethylamino-3-(3-methoxy-phenyl)-2-methyl-pentan-3-ol hydrochloride and oxybutynin, respectively, provided 21.7% and 10.7%, respectively, inhibition of the rate of bladder contractions. Thus, the additive effect of the combination of (+)-(2R, 3R)-1-dimethylamino-3-(3-methoxy-phenyl)-2-methyl-pentan-3-ol hydrochloride and oxybutynin would be expected to be 32.4%. However, administration of the combination provided 42.5% inhibition of the rate of bladder contractions. Thus, administration of the combination is 31% more effective than the additive effect of the compounds expected based on their action when administered alone. Accordingly, administration of the combination provides an unexpected synergistic (i.e. supra-additive) effect.

The test data demonstrating the unexpected synergistic effect is commensurate with the scope of the claims. The claims are directed to a combination of at least one 1-phenyl-3-dimethylamino-propane compound corresponding to formula I and oxybutynin. As discussed above, Example 1 shows an unexpected synergistic effect for the combination of (+)-(2R, 3R)-1-dimethylamino-3-(3-methoxy-phenyl)-2-methyl-pentan-3-ol hydrochloride and oxybutynin. The claims have been limited to the compounds of formula I in combination with oxybutynin, and the tested (+)-(2R, 3R)-1-dimethylamino-3-(3-methoxy-phenyl)-2-methyl-pentan-3-ol hydrochloride enantiomer is representative of the claimed 1-phenyl-3-dimethylamino-propane compounds of formula I. Accordingly, the test data for the combination of Example 1 is commensurate with the scope of the amended claims.

Applicants acknowledge that 0.1 mg/kg i.v. of (+)-(2R, 3R)-1-dimethyl-amino-3-(3-methoxy-phenyl)-2-methyl-pentan-3-ol hydrochloride and 0.03 mg/kg i.v. of oxybutynin were tested in Example 1. However, there is no reason to believe that the synergistic effect shown in Example 1 is limited to the particular dosages tested in Example 1. Indeed, synergistic effect is not typically dose dependent. Furthermore, the Office Action does not provide any reason that the

synergistic effect would be limited to the particular dosages tested. Accordingly, there is no need to limit the claims to the specific dosages tested because the tested composition is fairly representative of the now claimed invention defined by the amended claims, and the test data demonstrating a synergistic effect thus is commensurate with the scope of the claims.

For at least the reasons discussed above, withdrawal of the § 103(a) rejection over Chutka et al., Buschmann et al. '737, and Andersson et al. is respectfully requested.

Conclusion

In view of the foregoing amendments and remarks, the application is respectfully submitted to be in condition for allowance, and prompt, favorable action thereon is earnestly solicited.

If there are any questions relating to this Reply or the application in general, it would be appreciated if the Examiner could telephone the undersigned at (202) 624-2845 so that examination of this application may be expedited.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323 (Docket # 029310.53299US).

Respectfully submitted,

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